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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/193,538	11/17/98	BILLING-MEDEL	P 6193.US.P1

EXAMINER	
SOUAYA, J	
ART UNIT	**PAPER NUMBER**
1655	13

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DATE MAILED: 12/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

U.S. G.P.O. 1999 460-693

Office Action Summary

Application No.	Applicant(s)
09/193,538	Billing-Medel et al
Examiner	**Group Art Unit**
Jehanne Souaya	1655

☒ Responsive to communication(s) filed on *Sep 22, 2000*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-13, 15-22, 38, 41, and 45-49* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-13, 15-22, 38, 41, and 45-49* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Currently, claims 1-13, 15-22, 38, 41, and 45-49 are pending. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

3. Claims 1-13, 15-22, 38,41, and 45-49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims are drawn to polynucleotides, and methods of detecting the polynucleotides in a test sample as defined in the specification as products of a breast tissue gene designated as BS274 (pg. 10). The specification teaches the general utility for the invention is detection of the gene product itself in a sample. The specification does not teach a specific utility of the polynucleotides, genes and proteins whereby the invention would be a useful tool for a specific

purpose i.e. detection of itself in a sample detects the presence of a disease. The specification also does not provide any teachings as to the function of the encoded protein. The specification suggests that the invention may have substantial utility i.e. as an anti-BS274 antibody useful as a therapeutic agent (p. 52). However, the specification does not teach the therapy or demonstrate therapeutic results. Additionally, the specification suggests that the invention may have substantial utility i.e. the gene products may be useful for the diagnosis of a breast tissue disease or condition such as breast cancer by using the gene products to detect themselves in a tissue sample by hybridization (p. 63). However, the specification does not teach the diagnostic utility. Specifically, the specification teaches that the claimed gene products detect themselves in cancerous breast tissue. Additionally, the specification teaches that the BS274 was found in non-breast libraries (pg. 54, lines 20-25). Therefore, the specification does not teach a specific or substantial utility for the invention such that the invention would be useful to detect or treat a disease state. While the utility of gene products has been established in the art, applicants have not demonstrated a specific or substantial utility for the claimed invention.

Response to Arguments

The response traverses that the presence of BS274 was 28 time more prevalent in breast tissue than in the rest of the body and that the fact that a polynucleotide or protein is more prevalent in one tissue type than another means that it can be extremely useful as a cancer marker

for that tissue. The response cites PSA and CEA as examples. This argument has been thoroughly reviewed but was found non persuasive because the specification has not demonstrated that BS274 is a cancer marker for breast tissue. The specification has only taught that BS274 was found in breast tissue, but has not taught any examples which correlate the presence of BS274 with breast cancer as BS274 was found in normal breast tissue. While it is known in the art that PSA levels are elevated in prostate cancer, such an extrapolation cannot be made for BS274 as there is no teaching in the specification or the art that even suggest that BS274 and PSA are homologous, or have similar modes of action in cancer, or have similar functions, etc. Likewise, one cannot extrapolate that because CEA is found in blood at elevated levels in colorectal cancer, that the presence of BS274 outside breast tissue indicates a form of breast disease. While this could be an indication of breast disease, the specification has not shown that it is. The specification has only asserted that it is based on such characteristics of known cancer specific markers that are in no way related to BS274. Although such characteristics are established for other cancer markers, one cannot assume that such is the case for BS274 without a correlation of BS274 with breast disease, which the specification and the art fail to teach.

In addition, the response traverses that BS274 is related to a cytoskeleton associated protein known as CLIP-170 which is a microtubule binding protein involved in the binding of endocytic vesicles in microtubules. The response traverses that this is significant since malignant transformation involves abnormal changes in the cellular structures involving the cytoskeleton. The art, however does not teach that CLIP-170 is associated with cancer generally or breast

disease specifically. Furthermore, while the specification and the response suggest that the expression of BS274 in breast tissue suggests it could be useful in detecting diseases of the breast, the neither the specification nor the response teach how the homology of BS274 to CLIP-170 is associated with breast disease. It is noted that applicants have listed a sequence which is known in the prior art and which is homologous to the claimed sequence. Absent factual evidence, a percentage sequence similarity of less than 100% is not deemed reasonable to support one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. Although the high homology of BS274 to CLIP-170 suggests it could be a cytoskeleton associated protein, the specification provides no specific or substantial utility as to the use of BS274 in such a regard nor does the specification teach the function of the BS274 protein. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence homology results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding utility. (See Gerhold et al, Wells et al, and Russel et al). As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing...

a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claim Rejections - 35 USC § 112

Enablement

4. Claims 1-13, 15-22, 38, 41, and 45-49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The specification teaches that the compositions and methods described herein will enable the identification of certain markers as indicative of a breast tissue disease or condition, and that the information obtained therefrom will aid in the detecting, diagnosing, staging, monitoring, prognosis, in vivo imaging, preventing or treating diseases of the breast, however the specification does not teach having done so. It cannot be determined from the specification what the biological function of the polypeptides encoded by the sequences of SEQ ID NOS 1-7 nor how these polynucleotides or polypeptides are correlated to or would be useful in detecting any breast tissue diseases without undue experimentation. The teachings in the specification are an invitation to experiment.

Response to Arguments

Based on the examiner's response to applicants arguments made in the previous section, this rejection is maintained.

5. Claims 1-13, 15-22, 38, 41, and 45-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting the presence of a target BS274 polynucleotide consisting of SEQ ID NOS 1-7, and **the** complements of SEQ ID NOS 1-7, does not reasonably provide enablement for BS274 polynucleotides having 90% sequence identity with SEQ ID NOS 1-7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

It is well established that to claim a chemical compound, such as a polynucleotide, the inventor must be able to define the compound so as to distinguish the compound from other materials. The claimed compound must be defined in terms so as to provide a permanent and definite idea of the complete and operative invention. In the instant case, the claimed polynucleotides have not been clearly defined in terms of structure and/or function, and therefore one cannot make and use the polynucleotides as claimed. As stated in Vaek (CAFC 20 USPQ2d 1438, the "specification must teach those of skill in the art how to make and use the invention as broadly as it is claimed." However, in order to be able to make an invention, one must be able to clearly define that invention.

The claims are drawn to a method of detecting a polynucleotide having "at least 90% identity with" SEQ ID NO:s 1-7 and fragments and complements thereof (Claims 1-10) and to a gene which codes for an BS274 protein "which comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 17" (Claim 45). The specification teaches a single BS274 consensus polynucleotide, SEQ ID NO: 7, the sequence of which was assembled from 5 EST clones (SEQ ID NO:1-5) and the fill-length clone (SEQ ID NO: 7) (pg. 54).

Applicant's specification discloses a single BS274 gene sequence and a single BS274 protein sequence. Yet Applicant's claims, which are to sequences having "at least 90% identity" with a few sequences taught in the specification, may encompass thousands of polynucleotides. As discussed below, Applicant's definition of "% identity" is insufficient to provide a skilled artisan with the guidance necessary to clearly define the sequences encompassed by this claim language. Without specific teachings with respect to the methods used to determine "% identity", a skilled artisan could not be expected to identify or make the polynucleotides encompassed by the instant claims. Furthermore, irrespective of how "% identity" is defined, it is clear that by any definition of "% identity", may sequences encompassed by applicant's claims, and particularly those having "at least 90% identity" with fragments of the sequences taught in the specification, would bear little resemblance to the single BS274 consensus sequence that Applicant has taught. Neither the specification nor the claims set forth any particular structural or functional characteristics that a skilled artisan could use to identify polynucleotides that constitute BS274 polynucleotides, other than those described by SEQ ID NO. The term "BS274" is not an art

recognized term, and thus the prior art is silent with respect to structural and functional features that may be used to identify such polynucleotides. Furthermore, in teaching a single BS274 polynucleotide sequence and a single BS274 protein sequence, applicant clearly has not taught the isolation of a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. Thus, while the teachings of the specification and of the prior art would enable a skilled artisan to make polynucleotides consisting of SEQ ID NO: 1-7 and the complements of SEQ ID NO: 1-7, as well as polynucleotides encoding SEQ ID NO: 17, it is unpredictable as to whether a skilled artisan could make and use BS274 polynucleotides having "at least 90% identity" with SEQ ID NO: 1-7 and fragments and complements thereof, or genes encoding BS274 proteins having "at least 90% identity" with SEQ ID NO: 17. It would require undue experimentation for a skilled artisan to make and use the invention as broadly as it is claimed.

Response to Arguments

Applicants submit the software manual to the Wisconsin sequence analysis program as evidence of how to determine a specific per cent identity. This submission has been thoroughly reviewed but does not overcome the rejection. The term "BS274" is not an art recognized term, and thus the prior art is silent with respect to structural and functional features that may be used to identify such polynucleotides. Furthermore, in teaching a single BS274 polynucleotide sequence and a single BS274 protein sequence, applicant clearly has not taught the isolation of a

representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. Thus, while the teachings of the specification and of the prior art would enable a skilled artisan to make polynucleotides consisting of SEQ ID NO: 1-7 and the complements of SEQ ID NO: 1-7, as well as polynucleotides encoding SEQ ID NO: 17, it is unpredictable as to whether a skilled artisan could make and use BS274 polynucleotides having "at least 90% identity" with SEQ ID NO: 1-7 and fragments and complements thereof, or genes encoding BS274 proteins having "at least 90% identity" with SEQ ID NO: 17. It would require undue experimentation for a skilled artisan to make and use the invention as broadly as it is claimed.

Written Description

6. Claims 1-13, 15-22, 38, 41, and 45-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides wherein said polynucleotides have at least 90% identity with SEQUENCE ID NO: 1-7, and methods for using these polynucleotides to detect themselves (Claims 1-10). The claims broadly encompass full genes, genomic sequences, all allelic variants and mutant forms for the disclosed sequences which have not been described.

The specification teaches polynucleotides consisting of SEQ ID NO; 1,-7. However the specification does not teach the function of the polypeptides encoded by the polynucleotides of SEQ ID NOS 1-7. The specification also fails to teach how these polynucleotides are involved in breast tissue diseases. There is not adequate description of the genus of polynucleotides which have at least 90% identity with SEQ ID NOS 1-7. The claims broadly encompass full genes, genomic sequences, all allelic variants and mutant forms for the disclosed sequences which have not been described. There is substantial variability among the species of nucleic acids encompassed in the scope of the claim. The specification has also not defined a structural feature of the polynucleotides which would be common to all members of the genus that constitutes a substantial portion of the genus. Also, no description of the activity of function of the encoded protein has been described. Each of the claimed inventions is a genus for which a representative number of species must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims, sequences having at least 90% sequence identity with SEQ ID NOS 1-7, the specification fails to show that applicant was in fact "in possession of the claimed invention" at the time the application for patent was filed.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. No claims are allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Dec. 18, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600